Neurotransmission in Alzheimer's disease: a comprehensive paired pulse TMS investigation.

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INTRODUCTION

Alzheimer's Disease (AD) is **a** progressive neurodegenerative disease characterized by an impaired neurotransmission that affects primarily cholinergic but also ***glutamatergic, noradrenergic, gabaergic*** and ***dopaminergic*** systems. **Transcranial Magnetic Stimulation** (TMS) is a non-invasive brain stimulation tool able to investigate the functioning of intracortical circuits in humans. Different pharmacological studies have showed that modulations of these circuits could occur after neuro-active drugs administration and it could therefore be related to specific neurotransmitters. On the basis of these previous evidence we aimed to investigate neurotransmission in AD patients compared to a group of age-matched healthy-subjects (HS) using different paired pulse TMS (pp-TMS) protocol.

METHODS

Ten patients with a diagnosis of probable AD according to the NINCDS-ADRDA Criteria and 10 age-, sex- and education-matched HS were recruited for this study. We tested **Short Intracortical Inhibition** (SICI) and **Long intracortical inhibition** (LICI) to assess the functioning of gabaergic neurotransmission (respectively GABA-A and GABA-B), **Short intracortical facilitation** (SICF) to evaluate glutamatergic system and finally **Short-latency Afferent Inhibition** (SAI) protocols to explore cholinergic circuitry.

RESULTS

Data Analysis: Data were assessed measuring the percentage of change of peak-to-peak amplitudes of the mean MEPs produced by test stimulus alone compared to the mean MEPs produced by conditioned stimulus for each subject in each condition. Results showed that LICI was characterized by a decreased efficiency at ISI of 100 msec in AD patients compared to HS (**p=0.005**). SAI showed an impaired inhibition in AD patients compared to HS (**p=0.013**). No significant differences were found in SICF and SICI in AD patients compared to HS.

CONCLUSION

Our results provide evidence of an increased inhibition in long intra-cortical inhibition circuits as assessed by LICI protocol and of a reduced inhibition of cholinergic systems as shown by SAI in AD patients compared to HS.The current findings confirm that cholinergic circuitry is impaired in AD patients, but as well shed light on a possible involvement of GABA-B dysfunctions in pathophysiology of AD.

A.

AD	1	2	3	4	5	6	7	8	9	10
Age	77	64	65	73	77	74	74	76	64	55
MMSE	15.7	18.0	11.8	21.3	23	15.7	21	24.7	21	21

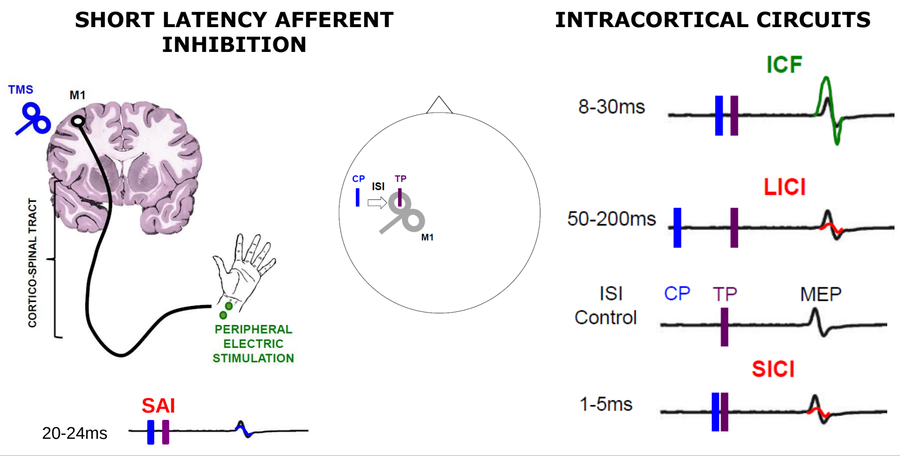
B.

HS	1	2	3	4	5	6	7	8	9	10
Age	59	67	62	73	68	77	74	65	72	58
MMSE	30	29	30	30	30	30	29	29	30	30

C.

	1 mV	rMT	p-Value
AD	55.6±13.4	46.8±9.6	0.22
HS	50.2±6.7	42.4±6.3	0.15

Mean age value and MMSE total score for AD patients (A) and HS (B) respectively. Threshold data of AD Patients and HS (C).



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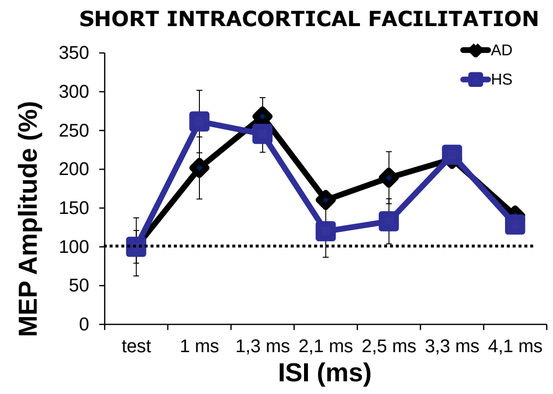

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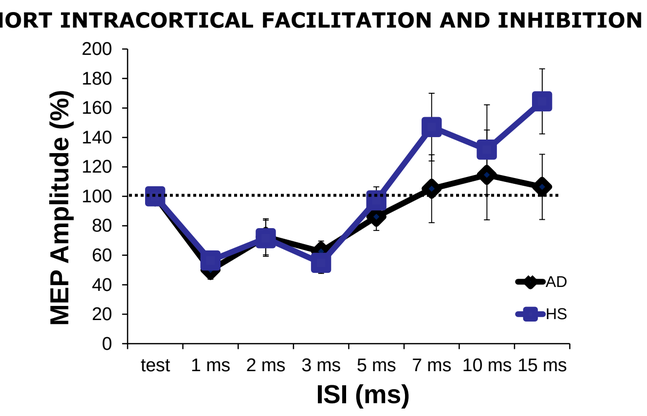

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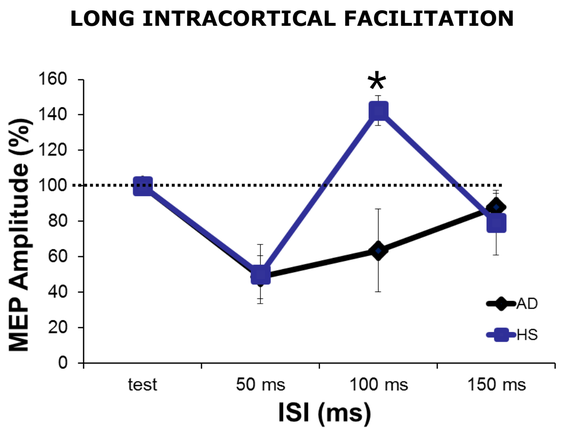

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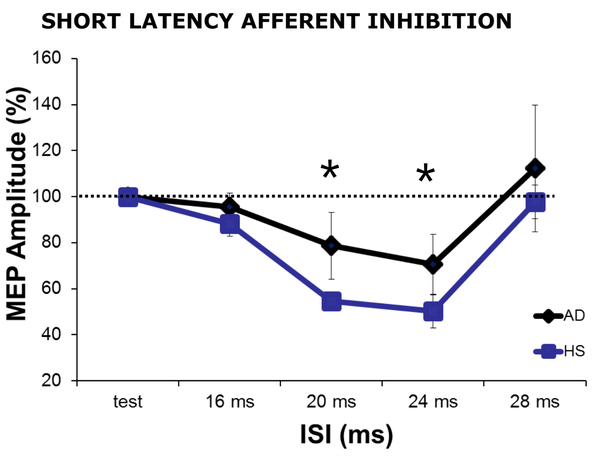

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